Author's response to reviews

Title: Effects of External Irradiation of the Neck Region on Intima Media Thickness of the Common Carotid Artery

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Author's response to reviews: see over
Dear Dr Picano,

the following are the answers to the questions by the reviewers for the manuscript entitled "Role of the external irradiation to the neck region on the intima media thickness of the common carotid artery” by M. Elena Gianicolo et al. The answers to the questions put by the first reviewer (Rosa Sicari) are highlighted in yellow while answers put by the second reviewer (Anca Corciu) are highlighted in turquoise.

Reviewer one (Rosa Sicari):

1. **Accepted**
   Please tone down the conclusions of the abstract section of the manuscript: IMT is not synonymous of disease but is an imaging biomarker related to the chance of developing disease.

2. **Accepted**
   In the background of the manuscript the paragraph before the aim of the study should be rewritten since it is well known the role of IMT as a risk factor and its relation with the development of cardiovascular events.

3. **Accepted**
   In the methods section of the manuscript the definitions of arterial hypertension, hypercholesterolemia etc. should refer to the conventional definitions and the relative references.

4. **Accepted**
   The major limitations of the study are related to the small patient population, the lack of the use of a quantitative method for the measurement of IMT and the short time between IMT assessment and radiotherapy. Please address.

5. **Accepted**
   Patient selection should be better detailed.

6. **Accepted**
   The results are presented in a quite confusing way. The conventional risk factors as well as age should be weighed when analyzing the increase of IMT.
As reported in the manuscript, we did not find any correlation between conventional risk factors and IMT in irradiated group. Moreover, it is interesting to note that a significant association between IMT and age (p < 0.0001) was found only in healthy adult controls and not in cancer survivors. On the contrary, the irradiated young patients showed higher IMT measurements than the non-irradiated young patients. However, we acknowledge that the limited sample size does not allow to emphasize the results.

7. **Accepted**

The discussion should have a paragraph on clinical implications. The recommendations given by authors should be toned down since the population is small and the routine assessment of IMT may not be sustainable.

**Reviewer two (Anca Corciu):**

1. **Accepted**

   Please correct the spelling mistakes from the entire paper.

2. **Accepted**

   Title: maybe it would be more appropriate the term of “effects” instead of the “role”.

3. **A) Accepted**

   Results:

   - please express the data as means ± standard deviation.

3. **B) Not accepted because the presence of plaque at the common carotid artery extending to the level of the bulb influence the measurements of IMT. Three significant carotid stenoses have been found.**

   You excluded from the study the patients with carotid plaque; it would be interesting to present these data, considering also the fact that the authors performed a “thorough scan of the extracranial carotid arteries for the eventual presence of carotid plaques, to increase sensitivity for identifying subclinical vascular disease”; how many significant carotid stenoses were found?

3. **C) Accepted**

   The study population consisted in patients with cardiovascular risk factors; please add some information about the therapy they are doing, such as antidiabetic therapy, lowering-lipid drugs, antihypertensive drugs…

3. **d) Accepted**
There are no statistically significant differences in the carotid intima medio-thickness compared with the side RT among patients who received symmetrical RT (left and right). When irradiation was partial IMT was greater, but the data is not statistically significant.

4. Accepted
Table 1: please add “years” as a measurement unit for age; please swap the order of the minimal and maximal value of age (lines 6 and 7; lines 17 and 18); correct the spelling mistakes (hypercholesterolemia, hypertriglyceridemia).

5. Accepted
Table 2: please add the legend and define “H”, “NH”, “RT”; please add the measurement unit for RT.

6. Please explain why you performed only 31 carotid IMT measurements instead of 38 (2 for each patient) for irradiated patients.
The irradiated carotid were 31, 7 were not even partially irradiated.

Yours sincerely,
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